International Journal of Trend in Scientific Research and Development (IJTSRD)
Volume 7 Issue 3, May-June 2023 Available Online: www.ijtsrd.com e-ISSN: 2456 – 6470

A Review on Nanogels

B. Karthikeyan[1], G. Alagumanivasagam[2]

[1]PG Student, Department of Pharmacy, Annamalai University, Tamil Nadu, India
[2]Assistant Professor, Department of Pharmacy, Annamalai University, Tamil Nadu, India

ABSTRACT

Nanogels are particles composed of physically or chemically cross-linked polymer networks that expand in an appropriate solvent. Nanogels are hydrophilic three-dimensional networks. Due to their relatively high drug-encapsulation ability, consistency, tunable size, effortless preparation, negligible toxicity, and stability in the presence of serum, including stimuli responsiveness, these studies integrate characteristics for topical drug delivery. These are soluble in water and permit immediate drug loading in aqueous media. These are created using a vast array of methods, including photolithographic technique, membrane emulsification, and polymerization methods. Due to the entrapment of nanoparticles in the gel matrix, nanogels used as dermatological preparations have prolonged exposure times on the skin, thereby extending the duration of therapeutic efficacy.

KEYWORDS: *Nanogels; Nanoparticles; Cross linkage; Polymerization; Antiseptic*

How to cite this paper: B. Karthikeyan | G. Alagumanivasagam "A Review on Nanogels" Published in International Journal of Trend in Scientific Research and Development (ijtsrd), ISSN: 2456-6470, Volume-7 | Issue-3, June 2023, pp.863-872, URL: www.ijtsrd.com/papers/ijtsrd57514.pdf

IJTSRD57514

I. INTRODUCTION

[Swati Talele, et al.] define nanogel as the nanoscale dispersion of hydrogel by physical and chemical cross-linking polymer. The size of nanogels varies between 20 and 200 nm [Bencherif SA et al]. Nanogels are three-dimensional hydrophilic networks that absorb significant amounts of water or physiological fluids without altering the structure's internal network [soni G et al.]. In addition to size-adjustability, a large surface area, and a high-water content, nanogels exhibit deformation and protruding properties. By using nanogels medications can be delivered in a prolonged and predetermined manner. Due to the three-dimensional structures of nanogels, it was simple to entrap pharmaceuticals, polymers, and dispersed liquid phases [Ankita Sharma et al]. The cavities of nanogels are capable of entrapping micro or macromolecules. They function as drug carrier molecules and are designed to readily incorporate biologically active compounds through the formation of biomolecular interactions such as salt bonds, hydrophobic or hydrogen bonding [Saurabh Tiwari et al.]. Nanogel exhibits properties between solids and liquids [Swati Talele et al]. When nanogels are utilised as a topical preparation, it is assumed that the entrapment of nanoparticles in the gel matrix will increase exposure time on the skin, thereby extending the duration of therapeutic efficacy [Inamdar Yashashri et al.]. It consists of a small number of solid components intertwined with polymers dispersed in a substantial quantity of liquid, with the solids forming a 3D network at the nanoscale level, resulting in a larger surface area for bioconjugation of active targeting sites. Nanogels can be administered as hydrophobic and hydrophilic medications, charged solutes, and additional diagnostic agents. This property was affected by the number of functional groups present in the network of polymer chains, the density of crosslinking, and the type of crosslinking agent present in the polymeric matrix. Nanogels were designed as polymeric micellar nanogels with gradual dissociation rates, adequate equilibrium over the surface-active agent micelles, lower critical micelle concentrations, and extended drug retention. They can be administered via oral, pulmonary, nasal, parenteral, intraocular, and other routes. The substance is released by photochemical internalisation that is pH-responsive, thermo sensitive, and volume-transition sensitive.

1.1. Advantages of nanogels [Hemant KS Yadav et al]

Nanogels are considered superior to other drug delivery systems for a number of factors, including:

1. **Biocompatibility and biodegradability:** Nanogel is manufactured from natural or synthetic polymers. Due to their high biocompatibility and biodegradability, accumulation in organs is prevented. The nanogel is prepared using Chitosan, methylcellulose, ethyl cellulose, and various polysaccharide-form polymers including dextran, pullulan, and dextrin. These polymers are biodegradable, stable, non-toxic, and hydrophilic.
2. **Swelling properties in aqueous media:** Nanogels have a strong affinity for aqueous solutions, resulting in their capacity to swell or reside, absorbing water when placed in an aqueous medium. This is the most advantageous characteristic of nanogels, as it gives them the greatest potential for the absorption and delivery of proteins, peptides, biomacromolecules, and bulky medications. Only when osmotic pressure is exerted by medium ions and there is an imbalance in the polymer's network swelling pressure does swelling occur.
3. **High drug loading capacity:** In comparison to conventional dosage forms, nanogels have a higher drug loading capacity. This is primarily due to the formulation's swelling property, which enables it to absorb an enormous quantity of water and provide sufficient cargo space to contain salts and biomaterials. A few additional factors also contribute to the high loading capacity, including the composition, molecular weight, the potential interactions between the drug and employed polymer, and the various functional groups present in each polymeric unit.
4. **Permeability and size** of particles owing to their nanoscale dimensions, surface charge, and hydrophobicity Nano lubricants are permeable to the skin: The reduced particle size, surface charge, and hydrophobicity of nanogels can significantly enhance permeability. Due to their small particle size, i.e., a diameter between 20 and 200 nm, they are capable of permeation by diffusion through tissues or endothelium, and in some cases through a specific transport system.
5. **Colloidal stability:** When manipulating nanoparticles, aggregation tends to occur, compromising colloidal stability. Increasing the zeta potential (minimum 30 mV) causes increased repulsive forces between particles, which electrostatically stabilises them. Other methods involve the incorporation of a surface modifier, such as polyethylene glycol (PEG), which generates steric effects and hydration forces to produce a stable nan suspension. This type of drug delivery system does not stimulate any immunological responses. Nanogels are nonimmunogenic in the circulation and the body's internal aqueous environment and do not provoke any immune responses.
6. **Ease of synthesis:** The synthesis of nanogels is a stress-free process that does not entail mechanical energy or harsh conditions. This method does not involve the use of organic solvents. Therefore, the drug can be easily loaded without being subjected to harsh conditions during the preparation process.
7. **High encapsulation stability:** In order to provide maximum therapeutic effects and minimal toxicity or adverse effects, the drug molecules loaded into the nanogel must be retained and not transported out or leak prematurely while circulating. **Controlled and sustained drug release:** To enhance the therapeutic efficacy of the drug and avoid its adverse reactions nanogels are formulated in such a manner that they are capable of releasing drugs in a pre-determined and prolonged pattern at the target site.
8. **Response to stimuli:** Nanogels can be used as a targeted drug delivery system and drugs can be targeted to a specific site without compromising its integrity, while dispersing to reach the target site and releasing the drug voluntarily in response to the appropriate stimulus.
9. **Targeting:** The nanogels can be used as a targeted drug delivery system by attaching to surface ligands, target determinants, or through "passive" targeting techniques, such as extravasation at pathological sites and retention in the microvasculature. The incorporation of ligands into nanogels through chemical modification results in targeted and triggered drug delivery and release.
10. **Low toxicity:** The nanogels must be highly biocompatible, free of toxicity, and biodegradable with non-toxic degradation products that are easily eliminated from the body.

1.2. Limitations of Nanogel

- Removing the surfactant and solvent at the end of the preparation procedure is costly.
- Debris of polymers or surfactants that persist in the body may have adverse effects.
- Limited drug-loading capacity and suboptimal drug release regulation

- The drug-polymer interaction may result in the disintegration of the structure, trapping the drug molecules irreversibly and enhancing the hydrophilicity of the nanogel matrix.

II. Applications of Nanogels [Swarnali D Paul et al]

Nanogels are established with great efficacy in the therapy of

- Cancer treatment
- Autoimmune disease
- Neurodegenerative disorders
- Diabetes
- Inflammatory disorders
- In stopping bleeding
- Used for delivering the drugs intracellularly
- Local Anesthetic
- Vaccine delivery
- Bone regeneration

III. Marketed Formulations of Nanogel [Pooja S mate et al]

The formulation of nanogels marketed list are mentioned the below table

NAME	USE	MANUFACTURED BY
Proxygeen nanogel	Relieve pain, Ankle pain Knee pain, Back pain	Wockhardt ltd
Oxalgw nanogel	Arthritis Low back pain Muscular pain	Zydus health care ltd
Nidret nanogel	Redule fine Wrinkles	Cadila health care ltd. (ZYDUS)
Litodol nanogel	Treatment of rashes	Madras pharmaceuticals
Ibugesil nanogel	Muscular pain, Joint pain	Golden cross pharma pvt.ltd.
Zeldinal nanogel	Pain relief	Leeford healthcare ltd. (India)
Nal nanogel	Treatment of acute pain	Systopic laboratories pvt. Ltd.
Satclin nanogel	Treatment of acne Reduce inflammation	Satyam healthcare (Tamil Nādu)
Sane care nanogel	Reduce accumulated fat on abdomen, arms.	Premium Medicare ltd
HA nanogel	Reduce bad breath	Optimum health care ltd
Zyelex	Erase the body pain	Noble pharmaceuticals ltd

IV. Classification of Nanogels

Nanogels can be categorised according to their cross-linking, response to stimuli (e.g., pH, temperature, light, ionic strength, etc.), and preparation techniques [Farhana sultan et al].

4.1. Classification of Nanogels based on their behavior towards specific stimuli.

Non-reactive nanogels: When non-reactive nanogels come into contact with water, they assimilate it, causing the nanogel to swell.

Stimulus-responsive nanogels: Environmental conditions, such as temperature, magnetic field, ionic strength, and pH, affect the degree of nanogel enlargement. Hence, the term stimuli-responsive nanogels. Multi-responsive nanogels are responsive to multiple stimuli.

4.2. Classification of Nanogels Based on the type of linkages of polymeric gel structure

1. **Physically cross-linked nanogels:** Also known as pseudo gels, these nanogels are highly dependent on the properties of the polymer used to create them, including polymer composition, temperature, polymer concentration, type of cross-linking agent, and ionic strength of the medium. This type of nanogels is formed by weak linkages such as Vander Waals forces, hydrogen bonding, or hydrophobic, electrostatic interactions. Several straightforward techniques permit the rapid production of nanogels with physical crosslinks. These procedures include the association of amphiphilic blocks, self-assembly, aggregation of polymeric chains, and complexation of polymeric chains with oppositely charged charges.
2. **Liposome-Modified Nanogels:** Liposome-modified nanogels are physically cross-linked, stimuli-responsive nanogels that are investigated as transdermal drug delivery devices due to their exceptional properties. These include the incorporation of poly [N-isopropyl-acrylamide] co-polymeric groups into liposomes, which results in a high degree of pH and temperature responsiveness.
3. **Micellar nanogels** are created by supramolecular self-assembly of hydrophilic and hydrophobic blocks or by graft copolymers in an aqueous solution. Micellar nanogels consist of a polymer-based hydrophilic shell (corona) encircling a hydrophobic core and stabilising the micelle as a whole. This conformation functions as a drug delivery system by physically trapping pharmaceuticals or biological macromolecules within the shell's borders.

4. **Hybrid Nanogels -** A Hybrid nanogel consists of nanogel particles dispersed in an organic or inorganic medium. Aggregation and self-assembly of amphiphilic polymers. Particularly as insulin and anticancer drug delivery systems, hybrid nanogels are of great importance.

5. **Chemically cross-linked** nanogels are formed by networks of strong covalent bonds and other permanent chemical links. The linkage strength is determined by the types of functional groups present in the nanogel network's molecules. To create this form of nanogels, polymeric chains are cross-linked at specific points, known as crosslinking points, which are determined by the available multifunctional crosslinking agent.

V. Synthesis of Nanogels Fundamental Criteria in NG Synthesis [Emanuele mauri et al]

Beyond the swelling behaviour, which can be categorised as a'superior' property of the NGs, the most important characteristics to consider in the synthesis of nanomaterials are biocompatibility, biodegradability, colloidal stability, surface area, loading capacity ensuring a prolonged and targeted drug delivery, and active/passive drug release due to the small particle size and surface properties. In addition, other features can be fine-tuned by meticulously regulating the NG synthetic routes.

- Release of both water-soluble and oil-soluble bioactive compounds.
- Versatility in route of administration.
- Reduced nanogel elimination and low immunogenicity by the mononuclear phagocytic system.
- Optimised nanogel permeability.
- Increase in the solvability of low-molecular-weight drugs.
- Decrease in the drug load compared to conventional drug administration.

5.1. Traditional NG Synthesis

Separated into chemical and physical strategies, nanogels can be synthesised. In general, the chemical synthesis produces nanonetworks with strong covalent bonds that improve the colloidal stability under in vitro and in vivo conditions, which is essential for preventing the leakage of the payload caused by the unintended dissociation of the gel network. These bonds can be distinguished into cleavable linkers based on the response to specific external stimuli (pH and temperature variations); stable bonds allow the gel to retain its conformation under Physico-chemical stress. Chemical crosslinking is the most advanced and versatile production method for NG. Physical assembly of NGs is a steady aggregation mechanism controlled by reversible Non-covalent bonds. Due to the lack of chemical reactions and the use of benign conditions in aqueous media, this method is more adaptable, despite the nanostructure's moderate fragility as a result of the nature of physical crosslinking.

1. Photolithographic Techniques

For drug delivery, photolithography was studied to create three-dimensional hydrogel particles or nanogel. This technique necessitates the development of surface treatment procedures for stamps or replica moulds to facilitate the release of moulded gels. There are five stages in photolithography.

- In the first stage, the UV cross-linkable polymer with low surface energy is emitted onto the photoresist-coated water that has been pre-baked.
- The polymer is shaped into designs on the silicon substrate using a quartz template and intense UV light.

2. Emulsion polymerization technique

Through the formation of monodisperse, kinetically stable particles in a continuous phase, emulsion-based polymerization occurs. The purpose of this procedure was to sustain polymerization in a confined space (the droplets), whose size would affect the final product's dimensions. The diffusion of organic droplets containing reactive monomers/polymers in an aqueous solution (oil-in-water, O/W emulsion) was referred to as direct emulsion polymerization, while the diffusion of aqueous droplets in an organic medium (water-in-oil, W/O emulsion) was referred to as inverse emulsification polymerization.

3. Membrane emulsification

This technique involves passing the dispersed phase through a membrane (glass or ceramic) with uniform pore size. Under specific conditions, emulsion particles or microgels with a specific morphology were formed on the surface of a membrane, which were then recovered by passing a continuous phase across the membrane. These manufactured emulsion nanoparticles can exist in a variety of emulsion formations, including water-in-oil (W/O), oil-in-water (O/W), oil-in-water-in-oil (O/W/O), and water-in-oil-in-water (W/O/W). The size of the formed droplet was determined by the pore size of the membrane, the velocity of the continuous phase, and the transmembrane pressure.

4. Precipitation polymerization

The homogeneity of the reaction system is a fundamental characteristic of precipitation polymerization. Before the reaction, all monomers, crosslinkers, and initiators are dissolved homogeneously in the same reaction medium. As the

polymerization reaction progresses, the polymer chain grows in length. The generated phase is separated to create polymer colloidal particles and then nanogels when the polymer chain reaches a certain length.

5. Dispersion polymerization

In this technique, the majority of ingredients, including monomers, chemical compound stabilisers, and initiators, are soluble in an organic solvent. Initially, the chemical process takes place in a highly gelled reaction mixture; however, the shaped polymers become insoluble in the continuous medium, resulting in the formation of a stable dispersion of chemical compound particles with the assistance of mixture stabilisers.

6. Photo-Induced Crosslinking Polymerization

Due to its bacteriostatic effect, additive-free nature, multifunctional nature, tunable particle diameter, and capacity to promote cross-linking, the application of irradiation in the formulation of nanogels is gaining popularity. Irradiation breaks water molecules into hydroxyl radicals and hydrogen atoms, which have the potential to convert polymers into micro radicals, resulting in intermolecular crosslinking and promoting nanogel formulation. Consequently, the viscosity of crosslinking can be modified by adjusting the laser's wavelength or power.

7. W/O heterogeneous emulsion method

W/O emulsion strategies typically entail Two actions: emulsification of binary compound particles of water-soluble biopolymers in continuous oil section using oil-soluble surfactants and cross-linking of biopolymers using soluble crosslinkers.

8. Reverse micellar method

This method entails a W/O dispersion, similar to the inverse (mini) emulsion method; however, a large amount of oil-soluble surface-active agents are utilised to form a thermodynamically stable micellar solution consisting of aqueous droplets dispersed in the continuous oil phase. The submicron diameter of the resulting micellar particles ranges from tens to hundreds of nanometers.

9. Inverse (mini) emulsion polymerization

- A W/O emulsion was formed from a mixture consisting of aqueous biopolymer droplets and a persistent oil phase using either a homogenizer or a high-speed mechanical stirrer.
- As a result, aqueous droplets of biopolymers are then crosslinked with appropriate crosslinking agents.

10. Inverse Microemulsion Polymerization

This method was investigated for the production of various nanogels. It produces microemulsions that are thermodynamically stable when an emulsifier is added above the critical threshold. Polymerization occurs within the aqueous droplets to produce stable hydrophilic and water- soluble colloidal nanoparticles with a diameter of 50–100nm.

5.2. living radical Polymerization [Farhana sultana et al]

Polymerization C-reactive protein has been investigated as a reagent for the synthesis of tightly regulated polymer–protein/peptide bioconjugates. The most successful techniques for C-reactive protein are atom transfer radical chemical process (ATRP), stable atom chemical process (SFRP), and reversible addition-fragmentation chain transfer (RAFT) chemical procedure.

1. Atom transfer radical polymerization

ATRP is the most widely used C-reactive protein technique, allowing the synthesis of a broad spectrum of polymers with the desired relative molecular mass and a relatively narrow relative molecular mass distribution (Mw/Mn 1.5). ATRP also enables the synthesis of copolymers with completely distinct chain architectures, such as block, comb-shaped, brush-shaped, and multi-star copolymers.

2. Reversible Addition fragmentation transfer (RAFT) process

A polymer undergoes a series of reactions with Di thioester compounds during RAFT; these include reversible addition, reversible degradation of adducts, and chain transfer reactions, which govern the molecular mass of the polymer during free radical polymerization. RAFT technology can transform the micelle structure of amphiphilic polymers by modifying the polymers' length, configuration, and properties.

VI. Drug Loading [Salim Meeran et al]

Nanogels are extensively used as carriers of therapeutic agents. A nano delivery system should possess a high drug-loading capacity, by reducing the required number of carriers. Drugs could be incorporated into nanogels by

- Covalent Conjugation
- Physical entrapment
- Self-assembly

1. Covalent conjugation

Biological agents were covalently conjugated during nanogel synthesis. For instance, enzymes modified with acrylic bodies were copolymerized with acrylamide using inverse microemulsion or diluted aqueous solutions to produce nanoscale hydrogels. Covalent conjugation of the drug with cross-linked nanogels provides the encapsulated drug with increased stability. By forming esters linkages, polysaccharides with hydroxyl groups readily interact

with the carboxyl group in the substance. In such cases, premature drug release may result from the cleavage of functional group bonds by enzymes such as esterase. In addition, by introducing readily cleavable linkers, degradable nanogels for a variety of applications were synthesized.

2. Physical Entrapment

Physical entrapment of proteins within cholesterol-modified pullulan nanogels and siRNA within HA nanogels. Furthermore, hydrophobic molecules can be incorporated into the nonpolar domain formed by nanogels' hydrophobic chains. In many instances, loading was accomplished through hydrophobic interaction between the drug molecules and the nanogel, resulting in relatively low loading levels (no more than 10%).

3. Self-Assembly

Self-assembly is the autonomous association of components into structurally well-defined aggregates. It has many advantageous characteristics, such as being cost-effective, versatile, and simple. This process takes place due to the thermodynamic minimums of the system, resulting in stable and robust structures. Diffusion is followed by the specific association of molecules via noncovalent interactions, including electrostatic and/or hydrophobic associations, to illustrate molecular self-assembly. Individually, these interactions are feeble, but the large number of interactions involved influences the structural and conformational behaviour of the assembly. While polysaccharides with opposing charges bind voluntarily due to electrostatic attractions, interactions between neutral polysaccharides are likely weaker or nonexistent, requiring the addition of chemical entities able to initiate assembly.

VII. Drug Release Mechanism of Nanogels

The liberation of drugs from nanogels at the targeted site of the action occurs in the following ways [Fateh AL Rahman et al].

- Simple diffusion of the drug from the nanogel
- Degradation of nanogel
- pH stimulus
- Ionic exchange with the environment
- External energy source

1. Simple Diffusion

The concentration difference between the environment and the gel results in the drug's diffusive release from the gel. The substance diffuses from a region with a higher concentration (within the gel) to a region with a lower concentration (the surroundings).

1. Nanogel degradation

The biodegradability of nanogels promises reduced toxicity and prevents unintended accumulation upon repeated administration. Incorporating easily cleavable bonds into the polymer backbone. Degradation occurs as a result of specific reducing compounds, pH, or even enzyme activity. Hydrophobic interaction encapsulation has decreased the rate of drug degradation.

2. pH-responsive mechanism

This mechanism is based on the fact that polymers used in the preparation of nanogels contain pH-sensitive functional groups that deionize within the polymeric network. The deprotonation causes an increase in the polymer's osmotic pressure, enlargement, and porosity, which initiates the release of the electrostatically bound molecules. Ionisation of pendant groups causes the pH-stimulated release from the gel. As implied by the term, drug discharge is sensitive to pH variations in the surrounding environment. The substance will be released at the optimal pH, which indicates that the release will occur primarily in a targeted area of the body that possesses this ph.

3. Displacement by ions present in the environment

Nanogel polymer is composed of anionic or cationic pendant groups. At the appropriate pH and ionic strength, these groups undergo ionization in aqueous environments. This generates a fixed charge on the polymer, resulting in electrostatic repulsion and the consequent enlargement of the gel's pores. Consequently, there was a greater inflow of water into the gel, resulting in nanogel enlargement and drug release. The substance can also be released via displacement with counterions. When a negatively charged drug-containing cationic nanogel interacts with negatively charged particles in the environment/cell surface, the drug is exchanged for the negatively charged particle.

4. Thermosensitive and volume transition mechanism

Few nanogels are reactive at specific temperatures referred to as the volume phase transition temperature, meaning they undergo a volume change in response to the temperature. If the adjacent channel is below the VPTT, the polymer becomes hydrated and quenched, simultaneously causing enlargement and releasing the drug-loaded polymer. In opposition to the VPTT, the nanogel abruptly contracts and the content flows out from above. In the past, thermos-responsive nanogels were used to rupture cellular networks when their size and volume increased.

5. Photoisomerization and Photochemical internalization

Photoisomerization is the process by which a limitedly rotatable bond endures some conformational changes when exposed to light. When photosensitizers are laden with nanogel, they generate two species of oxygen (singlet and reactive) that lead to the oxidation of cellular component walls, which affects the release of therapeutic agents into the cytoplasm.

The photothermal effect and a chromophore molecule bound to the polymer initiate the drug release. When the chromophore-containing nanogel was illuminated with light at its resonance wavelength, nonradiative relaxation converted the light energy into heat energy. The volume phase transition is observed due to the increase in temperature, which causes the substance to be released into the environment.

VIII. Preparation of Nanogels

The choice of preparation method is determined by the physicochemical properties of the polymer and substance to be loaded. The preparation of nanogels consists of the following procedures.

8.1. Emulsion-Solvent Diffusion Method [Swati talele et al]

The nanogel preparation from the Emulsion-Solvent Diffusion method involves the following steps.

The emulsification-solvent diffusion method is a technique for modifying the desalting procedure. Between a partially water-miscible solvent containing a polymer, a drug, and an aqueous solution containing a surfactant, a conventional O/W emulsion is formed. At room temperature, the polymer solvent and water are saturated, and then a large quantity of water is added to induce the diffusion of the solvent from dispersed droplets into the external phase. This causes the creation of particles. This method's benefits include increased encapsulation efficiency, simple enlargement, a narrow size distribution, and its simplicity. A large quantity of water and water-soluble drugs are removed from the suspension during the emulsification process and leak into the outer phase of the saturated aqueous phase, reducing the encapsulation efficiency.

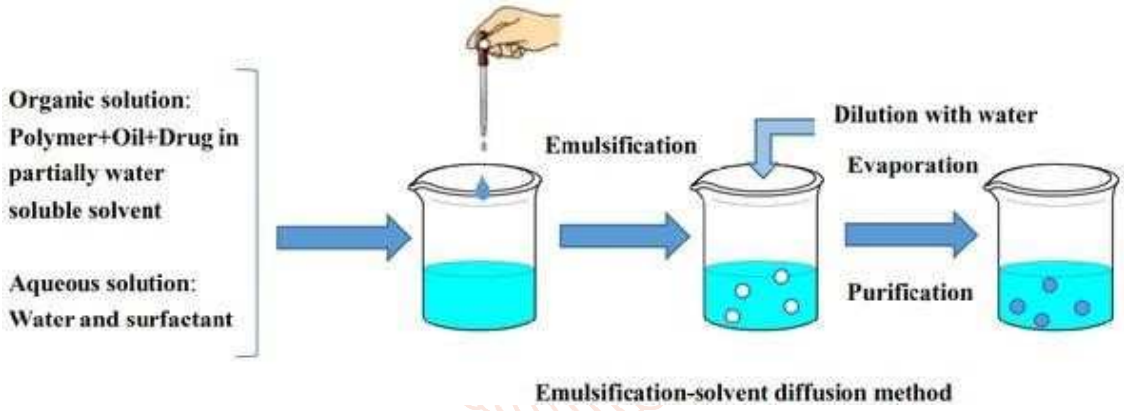

Figure 1 Emulsification-solvent diffusion method for the preparation of nanoparticles

8.2. Nano Precipitation Method [Ayesha Siddique Gazi et al]

Nanoprecipitation is also referred to as the solvent displacement technique. In a polar solvent, the polymer and substance are dissolved to form the organic phase. The solution is then added drop by drop to an aqueous solution containing an emulsifier or surfactant, resulting in the formation of nanoparticles due to the rapid diffusion of solvent.

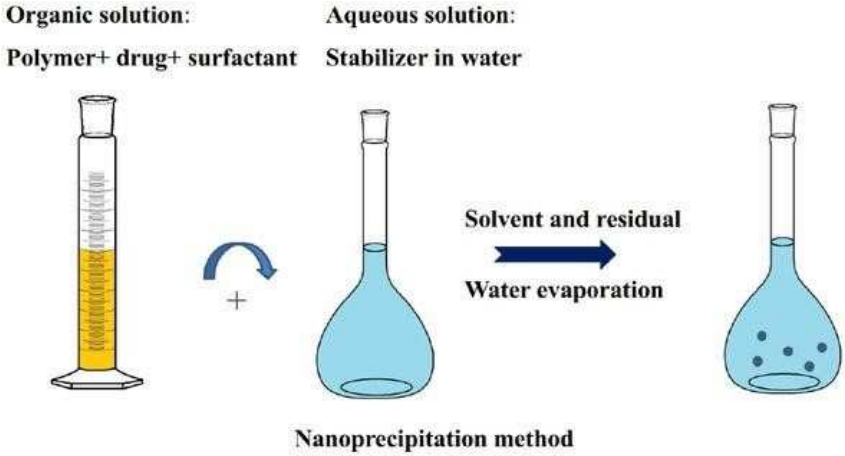

Figure 2. Nanoprecipitation method for the preparation of nanoparticles

8.3. Emulsion-solvent evaporation method [Dr. Prathima Srinivas et al]

Figure 3 depicts solvent evaporation techniques for the production of polymer-based nanoparticles. In a volatile solvent, a polymer solution is prepared, and an emulsion is formulated. As the solvent of the polymer dissipates, the emulsion transforms into a suspension, allowing the polymer to diffuse through the continuous phase of the emulsion. The single emulsion method prepares the emulsion oil (O) in water (W) by combining a polymer solution with water and a surfactant. The double emulsion technique is also referred to as the W/O/W technique. The method employs high-speed homogenization or sonication, followed by solvent evaporation at room temperature or under reduced pressure via continuous magnetic agitation.

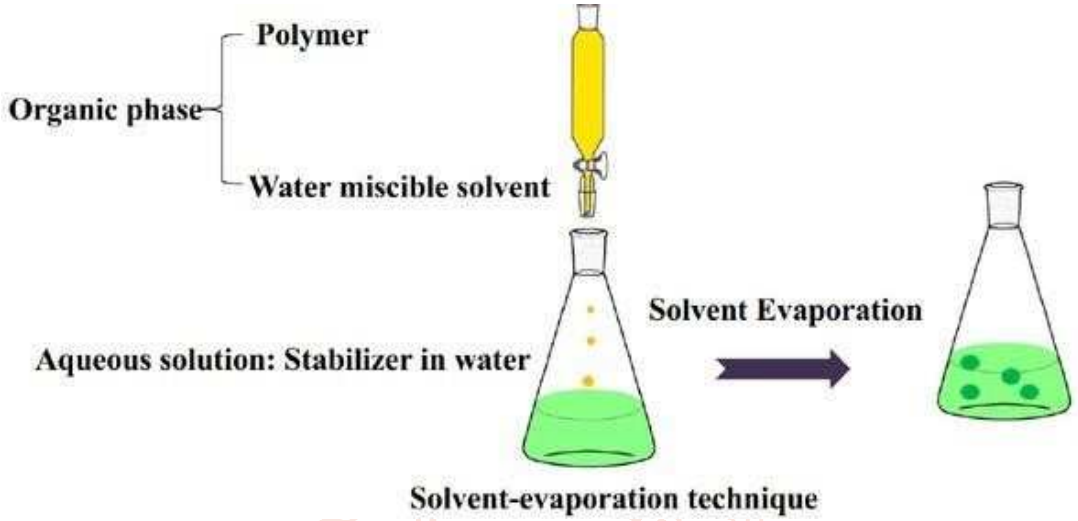

Figure 3. Solvent-evaporation technique for the production of nanoparticles

The solidified nanoparticles can be rinsed, collected by centrifugation, and lyophilized for long-term storage once the solvent has evaporated. The method can be performed simply in the laboratory, but it is only suitable for liposoluble drugs, as homogenization takes too much time and energy.

8.4. Reverse micellar method [Farhana sultana et al]

In an organic solvent, the polymer and drug applied to the surfactant are dissolved. Overnight, the crosslinking agent was added and agitated.

- After nanoparticles in the buffer have been purified, the solvent evaporates, resulting in the formation of a desiccated mass.
- The gelling agent was prepared by dissolving it in water. The obtained nanoparticles were combined with an aqueous phase containing a gelling agent, leading to the formation of nanogel.
- To neutralize the pH, pH adjuster was applied.

8.5. Modified emulsification - diffusion method [Chopade Swapnil et al]

- The drug was weighed and then combined with a polymer containing a solvent. This organic phase consists of the drug-polymer mixture added to the aqueous phase with constant agitation at 5000 to 10000 revolutions per minute. Using a syringe fitted with a needle, the organic phase was added to an aqueous stabiliser solution at a rate of 0.5 ml/min, drop by drop.
- The resulting dispersion was agitated for six minutes at 10,000-25,000 rpm and sonicated for five to ten minutes.
- In order to induce diffusion of organic solvent into a continuous phase, double-filtered water was added progressively to the dispersion with constant stirring for one hour.

IX. Evaluation of Nanogels [Muniraj SN et al]

Appearance

The nanogel bases were inspected visually for clarity, color, and appearance of any particles.

Homogeneity

The homogeneity was determined with the visual inspection of the nanogel formulation. They were tested for their appearance and the existence of any aggregates.

Measurement of particle size, polydisperse index, particle distribution

The mean size of the nanogels were measured by using Malvern Master Sizer 2000 MS and Zeta sizer, and values were recorded.

Determination of pH

The pH of the nanogel formulation was measured utilizing the digital pH meter Electrolab. A small quantity of formulation was moved to a beaker comprising a specific volume of purified water. The electrode was dipped into the formulation and the pH of nanogel was noted.

Drug content

The drug content present in the formulation was calculated using scanning through UV Spectrophotometer and High-performance liquid chromatography.

Spread ability.

This parameter of nanogel was determined by utilizing two slides (5 cm2). The 0.5g of the formulation was put in the middle of two slides and held aside for 1 min. The diameter of the spread circle of nanogel was measured and compared.

Infra-red spectroscopy

The IR spectrum of nanogels was obtained by using an FT-IR spectrophotometer, in the IR range of 4000-400 cm^{-1}.

SEM refers to scanning electron microscopy.

The surface morphology of nanogel formulation was determined by scanning electron microscopy at magnifications of X30, X500, X1000, and X3000 using a 20kV electron beam. Droplets of nanoparticulate dispersion of samples were placed on an aluminium metal plate and desiccated under vacuum to form a dry film, which was then observed using a scanning electron microscope.

Viscosity

The nanogel formulation's viscosity was measured using a Brookfield Rheometer with spindle number 64 and a speed of 10 rpm. The assembly was connected to a 25°C water receptacle that was thermostatically controlled and circulated. After determining the viscosity, it was introduced to the beaker encased in a thermostatic jacket. The spindle was allowed to move through nanogel, and the resulting values were recorded.

In-vitro drug discharge study

Utilising the Franz diffusion cell apparatus, the in-vitro drug release of the formulation was investigated. The formulation was distributed on a dialysis membrane positioned in the donor-receptor chamber of the Franz diffusion cell. The temperature was kept at 30 degrees Celsius. This assembly was agitated continuously using a magnetic field and magnetic stirring. The percentage of substance released from nanogel formulation was determined.

Stability analysis

Nanogel's accelerated stability was conducted in accordance with ICH guidelines. Assessing the stability of topical nanogel over three months at 25 2°C and 605% RH in an environmental stability chamber at 25 2°C and 605% RH. The formulation was transferred into amber-colored glass containers, which were then sealed and stored in the stability chamber. After three months, the consistency, drug content, and in-vitro drug release were measured.

X. Conclusion

Nanogel applications in targeted drug delivery, diagnosis, biosensing, and separation of biological substances have attracted significant research interest. Due to the small particle size of nanogels, the action or potency of the substance has been enhanced, as the smaller the particle size, the greater the surface area and, consequently, the greater the action. Nanogels possess the characteristics of both hydrogels and nanoparticles, which makes them a unique carrier system. The hydrogel properties allow nanogels to accommodate a large amount of water, which increases their drug loading capacities, imparts tissue-like properties, and makes them flexible. Nanogels have been established as potential targeting carriers that can deliver bioactive substances topically to the skin for conditions such as skin cancer, ulcers, inflammation, local anaesthesia, etc., based on the results of previous research.

XI. References

[1] Swati Talele, Preetam Nikam, Braja Ghosh, Chaitali Deore, Ashwini Jaybhave et al. (2017) A Research Article on Nanogel as Topical Promising Drug Delivery for Diclofenac sodium. Indian J of Pharmaceutical Education and Research 51(4S): 580-597.

[2] Bencherif SA, Siegwart DJ, Srinivasan A, Horkay F, Hollinger JO et al.(2009) Nanostructured hybrid hydrogels prepared by a combination of atom transfer radical polymerization and free radical polymerization. Biomaterial 30: 5270-5278.

[3] Soni G, Yadav KS (2016) Nanogels as potential nan medicine carriers for the treatment of cancer: A mini-review of the state of the art. Saudi Pharm J 24: 133-139.

[4] Ankita Sharma, Tarun Garg, Amrinder Aman, Kushan Panchal, Rajiv Sharma et al. (2014) Nanogel- an advanced drug delivery tool: Current and future. Arti Cells Nano med Biotech 44(1):165-177.

[5] Saurabh Tiwari, Shweta Singh, Pushpendra Kumar Tripathi, Chetan Kumar Dubey (2015) A Review- Nanogel Drug Delivery System. Asian J. Res. Pharm. Sci. 5(4):253-255.

[6] Swati Talele, Preetam Nikam, Braja Ghosh, Chaitali Deore, Ashwini Jaybhave, Anil Jadhav (2017) A Research Article on Nanogel as Topical Promising Drug Delivery. Indian J of

Pharmaceutical Education and Research 51(4S):

[7] Inamdar Yashashri (2018) Preparation and Evaluation of Nanogel: A Carrier Design for Targeted Drug Delivery System. Asian J Pharmaceutical Research Development 6 (3): 81-87.

[8] Farhana Sultana, Manirujjaman, Md. Imran-Ul-Haque, Mohammad Arafat, Sanjida Sharmin (2013) An Overview of Nanogel Drug Delivery System. J Applied Pharmaceutical Science 3(1): S95-S105.

[9] Hemant KS Yadav, Noor Anwar Al Halabi, Ghufran Ayman Alsalloum (2017) Nanogels as Novel Drug Delivery Systems - A Review. J Pharmacy Pharmaceutical Research 1: 50-83.

[10] Swarnali D Paul, Arvind K Jha (2017) Novel gels: implications for drug delivery. Nanostructures for Drug Delivery 379-412.